## **CLAIMS:**

10

15

**WO 2004/091395** 

- 1. A method for the spatially resolved determination of magnetic particle distribution, especially for the determination of, especially, physical, chemical and/or biological properties or parameters and/or changes in, especially, physical, chemical and/or biological properties or parameters within the area of examination of an object of examination by determining the changes in spatial distribution, concentration and/or anisotropy of the magnetic particles in this area of examination or in portions thereof in dependence on the effect of, especially, physical, chemical and/or biological influencing variables on at least a partial area and/or the, especially, physical, chemical and/or biological conditions in at least a partial area of the area of examination by means of the following steps:
- a) Introduction of magnetic particles in at least a portion of the area of examination in a condition that is irreversible or reversible, particularly periodically, modifiable or modified by, particularly, physical, chemical and/or biological influencing variables that affect the area of examination or by conditions at the area of examination,
- Generation of a magnetic field with a spatial distribution of the magnetic field strength such that the area of examination consists of a first sub-area with lower magnetic field strength and a second sub-area with a higher magnetic field strength,
- c) Change of the spatial location of both sub-areas in the area of examination so that the magnetization of the particles changes locally,
  - d) Acquisition of signals that depend on the magnetization in the area of examination influenced by this change, and
  - e) Evaluation of said signals to obtain information about the spatial distribution, concentration and/or permanent or temporary anisotropy of the magnetic

PCT/IB2004/050446 WO 2004/091395

21

particles in the area of examination.

- 2. A method as claimed in claim 2, characterized in that said conditions or parameters and/or external influencing variables are detected in an area of examination where the distribution and/or anisotropy of the magnetic particles changes or is changed in at least one portion of the area of examination.
- 3. A method as claimed in claim 1 or 2, characterized in that the magnetic particles in the condition in step a) generally have the same form, especially a round external form and/or such a form that the magnetic particles do not have a preferential direction from a magnetic aspect.
  - 4. A method as claimed in any one of the preceding claims, characterized in that the magnetic particles are enzymatically broken down or are metabolized.

- 5. A method as claimed in any one of the preceding claims, characterized in that the area of examination is subject to sound so that magnetostriction occurs in at least a portion of the magnetic particles.
- A method as claimed in any one of the preceding claims, characterized in 20 6. that the permanent or temporary change in anisotropy, especially the effective anisotropy, of the magnetic particle is detected.
- A method as claimed in any one of the preceding claims, characterized in 7. that the changes in spatial distribution and/or the permanent or temporary anisotropy of the magnetic particles detected in the area of examination are correlated with a local concentration, temperature, sound level and/ or a local pH value and/or the presence or absence of one or more enzymes.

WO 2004/091395 PCT/IB2004/050446

- 8. A method to improve resolution during the determination of the spatial distribution of magnetic particles in an area of examination with the following steps,
- a) Generation of a magnetic field with a spatial distribution of the magnetic field strength such that the area of examination consists of a first sub-area with lower magnetic field strength and a second sub-area with a higher magnetic field strength,
- b) Change of the spatial location of both sub-areas in the area of examination so that the magnetization of the particles changes locally,
- c) Acquisition of signals that depend on the magnetization in the area of examination influenced by this change, and
- distribution of the said signals to obtain information about the spatial distribution of the signals in the area of information, characterized in that a high frequency field is irradiated in the area of examination so that the temperature of the magnetic particle spin system is increased.
- A method as claimed in claim 8, characterized in that a high frequency field with a frequency in the range between circa 100 kHz to circa 100 GHz is radiated.
- 10. A method as claimed in any one of the preceding claims, characterized in that the magnetic particle is a mono-domain particle that can be reverse magnetized by

  Neel rotation and/or that the reverse magnetization is caused by Brownian rotation.
  - 11. A method as claimed in any one of the preceding claims, characterized in that the magnetic particle may be represented by a hard or soft magnetic multi-domain particle.
  - 12. A method as claimed in any one of the preceding claims, characterized in that the magnetic particles comprise hard magnetic materials.

WO 2004/091395 PCT/IB2004/050446

- 13. A method as claimed in any one of the preceding claims, characterized in that the hard magnetic materials comprise Al-Ni, Al-Ni-Co and Fe-Co-V alloys as well as barium ferrite (BaO 6xFe<sub>2</sub>O<sub>3</sub>).
- 5 14. Magnetic particle composition having a magnetization curve having a step change, the step change being characterized in that the magnetization change, as measured in an aqueous suspension, in a first field strength window of magnitude delta around the inflection point of said step change is at least a factor 3 higher than the magnetization change in the field strength windows of magnitude delta below and/or in the field strength windows of magnitude delta above the first field strength window, wherein delta is less than 2000 microtesla and wherein the time in which the magnetisation step change is completed in the first delta window is less than 0.01 seconds.
- 15 15. Magnetic particle composition according to claim 14, having narrow particle size distribution wherein at least 50 weight % of the particles have a particle size between plus or minus 50% of the average particle size.
- 16. Magnetic particle composition according to claim 14, wherein at least 50 weight % of the particles have a particle size between plus or minus 25% of the average particle size.
  - Magnetic particle composition according to claim 14, wherein the magnetic particles are mono-domain particles having an average particle size between 20 and 80 nanometres, wherein at least 50 weight % of the particles have a particle size between the average particle size plus or minus 10 nanometre
    - 18. Magnetic particle composition according to claim 17, wherein the monodomain particles having an average particle size between 40 and 60 nanometers.

24

- 19. Magnetic particle composition according to claims 14 to 16, wherein the magnetic particle is a multi-domain particle having substantially a needle shape having a demagnetisation factor of less than 0.001.
- Magnetic particle composition according to claim 14 or 15, wherein the magnetic particles comprise a non-magnetic core covered with a magnetic coating material, wherein the thickness of the coating is between 5 and 80 nanometres and wherein the demagnetisation factor is less than 0.01 and a diameter below 300μm.
- 10 21. Magnetic particle composition according to claims 14 to 20, wherein the time in which the magnetisation step change is completed in the first delta window is less than 0.005 sec.
- Magnetic particle composition according to claims 14-21, wherein the monodomain particles have a low magnetic anisotropy with a field needed for inducing Neel rotation of substantially below 10mT.
- 23. Magnetic particle composition according to claims 14-21, for application in medical magnetic particle imaging, wherein the step change occurs at a delta value below 1000 microTesla and the particle composition has a resolution value better than between 0.1 and 10 mm at magnetic field strength gradients between 10 and 0.1 T/m.
- Magnetic particle composition according to claims 14-23, wherein the height of the step change is at least 10% of the total magnetisation of the particle composition as measured at an external magnetisation field of 1 Tesla.
  - 25. Magnetic particle composition according to claim 14, wherein the magnetization change in the first field strength window of magnitude delta around the inflection point of said step change is at least a factor 4, preferably at least a factor 5 higher than the magnetization change in the field strength windows of magnitude delta

15

below and/or in the field strength windows of magnitude delta above the first field strength window.

- 26. Magnetic particle composition for imaging the viscosity in an area of the examination, wherein the magnetic particles are a magnetic particles according to any one of claims 14 to 25 and which particles have an anisotropy causing geometric rotation.
- Magnetic particle composition according to claim 26, wherein the internal anisotropy field in the particles is at least 0.1 mT, preferably at least 0.5 mT.
  - Magnetic particle composition according to claim 26, wherein the magnetic particle composition shows an opening in the hysteresis loop of the magnetisation curve of at least 0.1 mT, preferably at least 0.5 mT

Magnetic particle composition according to claims 14 to 28 for the measurement of a temperature in the examination area, wherein magnetic particles have a Curie temperature in a temperature range of interests in the examination area.

- 20 30. Magnetic particle composition according to claim 29, wherein the examination area is a living organism and wherein the Curie temperature is between 30 and 50 °C.
- 31. Magnetic particle composition according to claims 28 or 29, wherein the composition comprises at least two different parts therein the magnetic particles have a different Curie temperature.
  - Magnetic particle composition according to claims 14 to 28 for the measurement of a temperature in the examination area, wherein the magnetic particles

WO 2004/091395 PCT/IB2004/050446

have an anisotropy that is temperature dependant in a temperature window of interests in the examination area.

- Magnetic particle composition according to claim 32, wherein the composition comprises at least two different parts wherein the magnetic particles have a different temperature dependence of the anisotropy.
  - Use of a magnetic particle composition according to anyone of claims 14 to 33 in a method according to anyone of claims 1 to 9.

10

Use of the magnetic particle composition according to anyone of claims 14 to 33 in a method for the measurement of the viscosity or changes in the viscosity in a solidification process, for example the crystallisation solidification of a polymer material or the curing of a resin.

15

- An arrangement for carrying out the method as claimed in any of claims 8 to 13, comprising
- a) at least one device for generating a magnetic gradient field in at least one examination area of an examination object (A), said device comprising a means for generating a magnetic field with a spatial profile of the magnetic field strength such that there is produced in the examination area a first sub-area having a low magnetic field strength and a second sub-area having a higher magnetic field strength,
- b) means to change the spatial location of both sub-areas in the area of examination so that the magnetization of the particles changes locally,
  - c) high frequency generating means to generate a high frequency field to irradiate the area of examination such that the temperature of the magnetic particle spin system is increased,
- d) Means to acquire signals that depend on the magnetization in the area of examination influenced by this change,

e) Evaluation means for evaluating said signals to obtain information about the spatial distribution of the signals in the area of information.

37. An arrangement according to claim 36, wherein the frequency generated by the high frequency generating means is between 100 kHz and 100 GHz, preferably 10 to 100 MHz.